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Original Article

Prevalence of insulin resistance in obese adolescents

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Abstract

Background Childhood obesity is a global health problem, with the prevalence is differed in each country and affected by many factors, such as lifestyle and physical activity. Insulin resistance (IR) as a basic mechanism of several metabolic diseases in obesity, is related with metabolic syndrome (MetS) along with its long term complications, such as type 2 diabetes mellitus (T2DM). Several factors are known to be associated with IR, and the presence of acanthosis nigricans (AN) has an important meaning in predicting IR.

Objectives To assess the prevalence of IR, MetS in obese adolescents and its potentially associated factors, such as gender, signs of AN, and family history of metabolic diseases.

Methods A cross-sectional study was performed in obese adolescents, aged 12-15 years, over a two-month period. Fasting blood glucose, insulin, and lipid profiles were measured. Obesity was defined using body mass index (BMI). Insulin resistance was quantified by the homeostasis model assessment for IR (HOMA-IR). Metabolic syndrome was defined according to the International Diabetes Federation (IDF) 2007 criteria.

Results Of 92 obese adolescents, IR was found in 38% of subjects, with females predominating (57.2%). Signs of AN were seen in 71.4% of subjects and a positive family history of metabolic diseases was found in 82.8% of subjects, including family history of obesity, type 2 diabetes mellitus (T2DM), and hypertension. Less than 10% of subjects were considered to be in a prediabetic state, and none had T2DM. No statistical significance was found between gender, family history, or signs of AN and IR ($P>0.05$). Metabolic syndromes was found in 19.6% of subjects, with the following prevalences for each component: 34.8% for hypertension, 78.3% for central obesity, 8.7% for impaired fasting glucose (IFG), 22.8% for low levels of HDL, and 21.7% for high triglyceride levels. A strong correlation was found between IR and IFG with OR=5.69 (95%CI 1.079 – 29.993, $P=0.04$).

Conclusion We find a high prevalence of IR in obese adolescents, and IR increases the risk of prediabetes. Thus, prevention strategies are needed to overcome the long term impact of obesity on health. **[Paediatr Indones. 2013;53:167-72.]**

Keywords: *Obese adolescents, insulin resistance, metabolic syndrome*

Obesity during childhood and adolescence is a global health problem with differing prevalences among countries. Many factors affect obesity, such as ethnicity, gender, food habits, daily activity, and socioeconomic status, resulting in metabolic complications, such as type 2 diabetes mellitus (T2DM), glucose intolerance, and insulin resistance (IR).[1,2] Insulin resistance is the basic pathophysiology underlying MetS, with varying prevalences in different countries.[3,4] Ethnicity, age at onset of puberty, gender, birth weight, high blood pressure, history of obesity and T2DM in the family, and the presence of acanthosis nigricans (AN) may affect insulin sensitivity.[5-8] Long term complications associated with metabolic syndrome (MetS), such as

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T2DM, stroke and cardiovascular disease (CVD) rise in number in accordance with obesity.[9]

There are many techniques used to define IR, such as fasting insulin level, the homeostasis model assessment for IR (HOMA-IR), hyperglycemic-euglycemic clamp, and C-peptide measurement.[3,10-12] However, there is no single cut-off point used to define IR in children. We aimed to assess the characteristics of obese adolescents and factors associated with IR, such as gender, family history, and the presence of AN. We hypothesized that the prevalence of IR and MetS in an urban area like Jakarta would be high, and may be comprised of mainly females and adolescents with a family history of metabolic diseases, with the presence of AN as a predicting factor of IR.

Methods

This was a cross-sectional study performed on 92 obese adolescents, aged 12-15 years, from four junior high schools in Central Jakarta. We excluded children undergoing insulin or glucocorticoid therapy, those with acute infection at the time of testing, and those with T2DM or chronic illness that prevented completion of testing. All subjects' parents consented to participation. Study procedures were approved by the Ethics Committee of the Faculty of Medicine, University of Indonesia. Data collection was carried out between May and June 2012. Anthropometric measurements and blood testing were performed in the four schools at the start of the school day after an overnight fast (minimum fasting time of 10 hours). A questionnaire was used to collect information on demographics, medical history, medication use, complaints associated with obesity, and family history of any metabolic disease.

Anthropometric measurements included weight, height, and waist circumference (WC), and were measured with the subjects wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm. Weight was measured using a digital weight scale to the nearest 0.1 kg. Waist circumference was measured to the nearest centimeter using a non-stretchable tailor's measuring tape at the midpoint between the bottom of the rib cage and above the top of the iliac crest during minimal respiration. Acanthosis nigricans is a skin condition clinically characterized by dark, coarse, and thickened skin. It typically occurs in body areas where flexing, bending, and chafing of the skin by clothing occur, but is commonly and consistently found on the back of the neck.[13] Blood pressure was measured using a standard mercury sphygmomanometer with appropriate arm cuff length, with the subject seated and the arm at heart level, after at least 5 minutes of rest. The mean of two determinations was used to express an individual's systolic and diastolic blood pressures.

All biochemical measurements were carried out by the same team of laboratory technicians with the same methods throughout the study period. Blood specimens were transported to the Prodia laboratory directly for evaluation of blood glucose, insulin and lipid profiles [high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides (TG)].

Body mass index was calculated as the ratio of weight (kg) to height squared (m^2), and standardized for sex and age charts from the Centers for Disease Control and Prevention.[14] Obesity was defined as BMI ≥95 percentile specific to age and sex. Insulin resistance was measured using the HOMA-IR (fasting level of insulin (μU/mL) x fasting glucose (mMol/L) / 22.5) and considered to be present in subjects with scores ≥ 3.8.[3] Metabolic syndrome was defined according to the International Diabetes Federation (IDF) criteria.[15] For children aged 10-15 years, a diagnosis of MetS was made if abdominal obesity was present (WC ≥90th percentile or adult cut-off, if lower) and the presence of two or more other components: elevated TG (≥1.7 mmol/L or ≥150 mg/dL), low HDL (<1.03 mmol/L or <40 mg/dL), high blood pressure (systolic ≥130mmHg or diastolic ≥85mmHg), and elevated fasting blood glucose (≥5.6 mmol/L or 100 mg/dL). Dyslipidemia was diagnosed in subjects with a combination of high TG, low HDL, and high LDL levels.[16]

Data was analyzed using the Statistical Package for Social Sciences software (SPSS Inc., Chicago, IL, USA) version 17. Subjects' characteristics were described using percentages. Bivariate test was performed to assess associations between independent and dependent variables for the risk factors, and continued with multivariate analysis for results that fit the criteria. Chi-square test was used in this analysis, however, Fisher's test was an alternative test for paired nominal variables, or Mann-Whitney test for paired numeric and nominal variables. A P value of less than 0.05 was considered to be statistically significant.

Results

This study included a total of 92 subjects (42 boys and 50 girls) aged 12-15 years. Descriptive characteristics of all subjects are presented in **Table 1**. Subjects' symptoms related to obesity are presented in **Table 2**.

The mean fasting insulin was 20.2 μU/mL, with a median HOMA-IR of 3.1, and a mean HOMA-IR of 4.6. Insulin resistance (HOMA-IR ≥3.8) was found in 35 (38%) subjects. **Table 3** shows the characteristics of the subjects with IR.

Of the 35 subjects with IR, 3 (8.6%) subjects had impaired fasting glucose (IFG), but none had T2DM. All subjects with IFG were boys, within BMI range 30 – 39.9, and had AN. Factors associated with IR are shown in **Table 4**. We found that none of the risk factors for IR were significantly associated with IR in our subjects.

Table 1. Subjects' characteristics

Characteristics	n (%)
Family history*	
T2DM	18 (19.6)
CVD	6 (6.5)
Stroke	2 (2.2)
Hypertension	30 (32.6)
Obesity	58 (63)
None	20 (21.7)
Acanthosis nigricans	
Positive	66 (71.7)
Negative	26 (28.3)

Note:* Each subject may have family history of ≥1 illness

Table 2. Symptoms experienced by subjects

Symptoms	n
Snoring	7
Breathing difficulty	18
Easily fatigued	5
Joint pain	2
Chest pain	3
Acne	10
No complaints	60

Table 3. Characteristics of subjects with insulin resistance

Characteristics	n (%)
Gender	
Male	15 (42.8)
Female	20 (57.2)
Family history*	
T2DM	6 (17.1)
CVD	3 (8.6)
Stroke	0
Hypertension	12 (34.3)
Obesity	24 (68.6)
None	6 (17.1)
Acanthosis nigricans	
Positive	25 (71.4)
Negative	10 (28.6)

Note:* Each subject may have family history of ≥1 illness

The prevalence of MetS was 19.6%, with more affected girls than boys (11 girls vs. 7 boys). The prevalences of the MetS components were 34.8% for hypertension, 78.3% for central obesity, 8.7% for IFG, 22.8% for low HDL levels, and 21.7% for high TG levels.

Dyslipidemia was found in 4 (4.3%) subjects.

Table 4. Factors associated with insulin resistance

	Insulin resistance				
	Positive n=35	Negative n=57	P value	OR	95% CI
Gender, n (%)			0.673	1.2	0.514 to 2.801
Male	15 (42.8)	27 (47.4)			
Female	20 (57.2)	30 (52.6)			
Family history of metabolic diseases, n (%)			0.646	1.289	0.435 to 3.816
Yes	29 (82.8)	43 (75.4)			
No	6 (17.2)	14 (24.6)			
Family history of obesity, n (%)			0.579	1.273	0.521 to 3.111
Yes	24 (68.6)	34 (59.6)			
No	11 (31.4)	23 (40.4)			
Family history of T2DM, n (%)			0.646	0.776	0.262 to 2.297
Yes	6 (17.1)	12 (21)			
No	29 (82.9)	45 (79)			
Family history of hypertension, n (%)			0.788	1.13	0.462 to 2.764
Yes	12 (34.3)	18 (31.6)			
No	23 (65.7)	39 (68.4)			
Acanthosis nigricans , n (%)			0.959	0.976	0.384 to 2.482
Positive	25 (71.4)	41 (71.9)			
Negative	10 (28.6)	16 (28.1)			

Table 5. The relationship of IR with each component of metabolic syndrome

Components	P value	OR (95% CI)
Fasting glucose ≥100 mg/dL	0.05	5.690 (1.079 to 29.993)
Hypertriglyceridemia	0.213	1.880 (0.690 to 5.120)
Low HDL level	0.996	1.003 (0.368 to 2.773)
Central obesity	0.402	1.574 (0.542 to 4.570)
Hypertension	0.710	1.182 (0.490 to 2.848)
High LDL level	0.636	0.811 (0.340 to 1.931)

Table 6. Multivariate analysis of IR with components of metabolic syndrome

	Variables	Coefficient	P value	OR	95% CI
Step 1	Fasting glucose ≥100 mg/dL	1.669	0.051	5.309	0.995 to 28.329
	Hypertriglyceridemia	0.535	0.312	1.707	0.606 to 4.811
	Constant	-0.754	0.004	0.470	
Step 2	Fasting glucose ≥100 mg/dL	1.739	0.040	5.690	1.079 to 29.993
	Constant	-0.640	0.005	0.527	

However, high cholesterol LDL (>100 mg/dL) was found in 58 (63%) subjects. **Table 5** and **Table 6** show the relationship of IR with each component of MetS.

Discussion

We present data on IR and MetS in obese adolescents. In our study, we used HOMA-IR to assess for IR in obese subjects. Several past investigations have shown that HOMA-IR is both valid and reliable used in pediatric populations.[3,17] The prevalence of IR was 38%, with a majority of girls, and most IR's subjects had histories of obesity, hypertension, and T2DM in the family. Also, the majority of IR subjects had AN. None of the probable associated factors, such as gender, family history, or the presence of AN were significantly associated with IR (P>0.05) in our subjects. The prevalence of IR in our study was similar to those reported in Pakistan (35%)[18] and Bolivia (40%).[3] However, previous studies found that IR was more predominant in boys during adolescence than in girls.[19-21] The reason for our having more girls with IR was unclear.[22]

Family histories were based on self-reports. Siddiqui *et al*. found no statistical significant relationship between IR and family history of T2DM (P=0.08), as well as between IR and hypertension (P=0.6). However, having a family history of T2DM might raise the risk of IR three times.[18] Another study found that fasting insulin level was associated with a family history of T2DM (r=0.336; P<0.05), fat mass (r=0.572; P<0.001), and waist circumference (r=0.553; P<0.001).[23]

We found that 71.4% of our subjects with IR had AN, however, there was no significant association found between them (P>0.05). Our results were similar to those in previous studies.[3,23,24] Tirtamulia *et al*. found that 82% of young obese children with IR had AN, however, the correlation between them was weak (r=0.57).[25] Kobaissi *et al*. showed that AN had a negative correlation with insulin sensitivity (r=-0.45–0.61, P<0.01).[13] Acanthosis nigricans appears as an early manifestation of obesity syndrome. In addition, AN helps to identify the risk of dyslipidemia, hypertension, and IR, as well as serving as a useful tool for health screening and prevention.[26]

There is increased prevalence of impaired glucose tolerance in obese children and this is associated with IR and the impairment of insulin sensitivity. Within a two-year study, children with IR were found to proceed to T2DM even with proper management.[27] Our study found that 8.6% of subjects were already in a prediabetic state (using IFG), but none had T2DM.

Insulin resistance and obesity have been identified as the main features of MetS. Many definitions have been used to describe MetS, such as those from the National Cholesterol Education Program's Adult Treatment Panel III, the European Group for the Study of Insulin Resistance, and the IDF 2007.[15,16,28] Using the pediatric IDF definition

for children aged 12-15 years, we found 19.6% of the adolescents had MetS. The majority of our subjects also had hypertension (34.8%), although results differ among countries.[3,29,30]

Metabolic syndrome is an important risk factor for atherosclerosis in CVD. Cardiovascular disease is also affected by IR, high blood pressure, obesity, and dyslipidemia.[31] Dyslipidemia in obesity was found in 4.3% of our subjects, much lower than that of previous studies.[32,33] The combination of obesity and dyslipidemia increases the negative effect of atherosclerotic lesions in young adults.[33] IR and high levels of insulin increase the risk of MetS in several ethnicities.[34] In our study, we did not analyze ethnic differences. IR increased the risk of IFG almost six times, but it did not increase the risk for hypertension, hypertriglyceridemia, or low HDL levels ($P>0.05$). Several studies found results different from ours.[18,24]

In conclusion, our results indicate that the prevalence of IR in Jakarta is high among obese adolescents. In addition, although the MetS prevalence is low, a high proportion of children have hypertension. Having a family history of T2DM does not increased the risk of IR.

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